State of California

M e m o r a n d u m

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To: Gary Patterson, Chief
Medical Toxicology Branch

Date July 5, 1996
Place Sacramento

From **Department of Pesticide Regulation** - John M. Donahue, Chief
Worker Health and Safety Branch

Subject Revised Policy on Dermal Absorption Default for Pesticides

For many years both U.S. EPA and DPR have used 100% as the default dermal absorption for a pesticide in the absence of compound specific experimental data. Over the past eight years, the branch has had the opportunity to review many rat dermal absorption studies. I would estimate the number of different active ingredients reviewed at about 40. However, Robert Zendzian at U.S. EPA recently wrote that he had reviewed dermal absorption studies for over 100 active ingredients. From our review experience, we feel that a change in default dermal absorption is warranted.

Based upon reviews conducted up to 1993 (the last time we compiled all the results available) (Thongsinthusak *et al.*, 1993), we had reviewed rat studies for 26 active ingredients. Since that time we have evaluated 14 more studies (Thongsinthusak, 1996; personal communication). The mean rat dermal absorption from several different chemical classes for 40 compounds was 19 $\pm$ 14%. Thus at the 95th percentile, dermal absorption for pesticides in general is ~42%, and our current default overestimates the reasonable upper bound by more than two fold.

The purpose of having a high default value for dermal absorption is to encourage registrants to produce quality dermal absorption studies when the default may not provide an adequate margin of safety. Another benefit is that when we err it is on the side of safety. By reducing the default to 50%, there is still incentive, but the default becomes more credible because it is at the high end of values that typically occur in rats. It is still a very safe assumption, because we know that rats typically overestimate human dermal absorption by two to ten fold (Wester and Maibach, 1993). We are not aware of any pesticide that is 100% absorbed in humans.

With two laboratories in California alone (Howard Maibach's at UCSF and Sami Salim's at McGaw in Irvine) as well as laboratories in both the Netherlands and England willing to conduct ethical human dermal absorption studies at costs approximating a rat study, we feel very strongly that the regulated community would be best served with a human dermal absorption estimate. Not only is human dermal absorption data typically lower than rat dermal data, but also humans are the species that will be exposed under actual use conditions.

[original signed by John Donahue, Branch Chief]

For scoping purposes (as opposed to regulatory purposes), or in the case of emergency, dermal absorption can be estimated by the method of Durkin *et al.,* (I 995). This article suggests that for pesticides with log Kow > 1. 85, we can estimate human dermal absorption with the equation (log % applied dose absorbed/day = -0.005 x molecular weight + 2. 1).

With this memorandum, we will commence moving away from the 100% default for dermal absorption to a more rational 50%. Some of our sister departments in Cal/EPA are using 10-25% defaults for dermal absorption of organic compounds already, and this would also bring us into closer conformance with them.

References:

Durkin, P. R., Rubin, L., Withey, J., and Meylan, W. 1995. Methods of assessing dermal absorption with emphasis on uptake from contaminated vegetation. *Toxicol. Ind. Health.* 11: 63-79.

Thongsinthusak, T., Ross, J., Sanborn, J, and Wang, R. 1992. Dermal absorption of pesticides in animals and humans. VVH&S, DPR. HS-1676 (March 19, 1993). A poster presentation at the 205th ACS Meeting, March 28-April 1, 1993, Denver, Colorado.

Thongsinthusak, T. 1996. Results of dermal absorption studies of 14 pesticides in rats. WH&S, DPR (Personal communication).

Wester, R. C., and Maibach, H. 1. 1993. Animal models for percutaneous absorption. In *Health Risk Assessment: Deri7ial and Inhalation Exposure and Absorption of Toxicants,* eds. R. G. M. Wang, J. B. Knaak, and H. 1. Maibach, chapter 5, pp. 89-105. London: CRC Press.

cc: Tom Thongsinthusak
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